Safety Data Sheet

N-Nitroso-N-ethylurea

Division of Safety
National Institutes
of Health

WARNING!

THIS COMPOUND IS TOXIC, CARCINOGENIC, MUTAGENIC, AND TERATOGENIC. ALKALINE HYDROLYSIS PRODUCES DIAZOETHANE, WHICH IS A HIGHLY TOXIC, IRRITATING, CARCINOGENIC, HIGHLY FLAMMABLE, AND EXPLOSIVE GAS.

LABORATORY OPERATIONS SHOULD BE CONDUCTED IN A FUME HOOD, GLOVE BOX, OR VENTILATED CABINET.

AVOID SKIN CONTACT: IF EXPOSED, WASH WITH SOAP AND COLD WATER. AVOID RUBBING OF SKIN OR INCREASING ITS TEMPERATURE.

FOR EYE EXPOSURE, IRRIGATE IMMEDIATELY WITH LARGE AMOUNTS OF WATER. FOR INGESTION, DRINK MILK. REFER FOR GASTRIC LAVAGE. FOR INHALATION, REMOVE VICTIM PROMPTLY TO CLEAN AIR. ADMINISTER RESCUE BREATHING IF NECESSARY. REFER TO PHYSICIAN.

IN CASE OF LABORATORY SPILL, WEAR PROTECTIVE CLOTHING DURING CLEANUP. WASH DOWN AREA WITH SOAP AND WATER. DISPOSE OF WASTE SOLUTIONS AND MATERIALS APPROPRIATELY.

A. Background

N-Nitroso-N-ethylurea (ENU) is toxic, carcinogenic, mutagenic, and teratogenic in animals and experimental test systems. Its primary use is for tumor induction and related research in experimental animals and as a research mutagen.

B. Chemical and Physical Data

1. Chemical Abstract No.: 759-73-9

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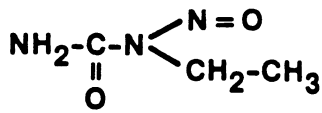
Synonyms:

ENU	1-Ethyl-1-nitrosourea
NEU	N-Nitrosoethylurea
Ethylnitrosourea	Nitrosoethylurea
N-Ethyl-N-nitrosourea (9CI)	

Molecular formula: $C_3H_7N_3O_2$

structure: 

weight: 117.1

Density: No data.

Absorption spectroscopy: IR, UV, NMR spectra have been reported by Heyns and Roper (1974). UV (CH_2Cl_2): λ (log ε) = 237 (3.85), 401 (2.08), and 418 (2.04) (Mirvish, 1971).

Volatility: No data. May be nonvolatile by analogy with N-nitroso N-methylurea (Mirvish et al., 1976).

Solubility: Approximately 1.3% in water at room temperature. Soluble in polar organic solvents.

Description, appearance: Yellow to pink crystals.

Boiling point: No data.

Melting point: 102-104°C (with decomposition).

Stability: The pure compound is sensitive to humidity and light and should be stored in the dark at less than -10°C in tightly closed containers protected from moisture. Stability in aqueous solution is pH dependent, with maximum stability occurring at about pH 4 (Druckrey et al., 1967).

Chemical reactivity: ENU is an alkylating agent. It is hydrolyzed by strong alkali (liberating diazoethane, a highly toxic gas) and by strong acid.

Flash point: Does not apply.

Autoignition temperature: No data.

Flammable limits: Does not apply.

re, Explosion, and Reactivity Hazard Data

Dry chemical or carbon dioxide extinguishers may be used. Fire fighters should wear air-supplied respirators with full-face masks.

Decomposition products may be explosive. Sealed bottles at room temperature may explode due to gas pressure.

Sensitive to light and moisture.

Incompatible with water.

Alkaline hydrolysis produces diazoethane, which is a highly toxic, irritating, flammable, and explosive gas.

Avoid contact with alkaline solutions.

rational Procedures

NIH Guidelines for the Laboratory Use of Chemical Carcinogens
cribe operational practices to be followed when potentially
cinogenic chemicals are used in NIH laboratories. The Guidelines
uld be consulted to identify the proper use conditions required
specific controls to be implemented during normal and complex
rations or manipulations involving ENU.

Chemical inactivation: No validated method reported.

Decontamination: Turn off equipment that could be affected by ENU or the materials used for cleanup. If more than 1 g has been spilled or if there is any uncertainty regarding the procedures to be followed for decontamination, call the NIH Fire Department (dial 116) for assistance. Wash surfaces with copious quantities of water. Glassware should be rinsed (in a hood) with a polar organic solvent, followed by soap and water. Animal cages should be washed with water.

Disposal: No waste streams containing ENU shall be disposed of in sinks or general refuse. Surplus ENU or chemical waste streams contaminated with ENU shall be handled as hazardous chemical waste and disposed of in accordance with the NIH chemical waste disposal system. Nonchemical waste (e.g., animal carcasses and bedding) containing ENU shall be handled and packaged for incineration in accordance with the NIH medical-pathological waste disposal system. Potentially infectious waste (e.g., tissue cultures) containing ENU shall be disinfected by heat using a standard autoclave treatment and packaged for incineration, as above. Burnable waste (e.g., absorbent bench top liners) minimally contaminated with ENU shall be handled as potentially infectious waste and packaged for incineration, as above. Absorbent materials (e.g., associated with spill cleanup) grossly contaminated shall be handled in accordance with the chemical waste disposal system.

Radioactive waste containing ENU shall be handled in accordance with the NIH radioactive waste disposal system.

4. Storage: Store working quantities of ENU and its solutions in a safety refrigerator in the work area. Store stocks of ENU below -10°C in amber bottles with caps and Teflon cap liners. Do not store in ampoules since these could explode. Avoid exposure to light and moisture.

Monitoring and Measurement Procedures Including Direct Field Measurements and Sampling for Subsequent Laboratory Analysis

1. Sampling: ENU could be found in aerosols formed in the laboratory, but no reliable sampling method for this potential hazard has been reported.

2. Separation and analysis: HPLC and TLC are appropriate for separation of nitrosamides. UV spectrophotometric detection has been used with HPLC (Heyns and Roper, 1974) and TLC (Mirvish and Chu, 1972) for detection and quantitative determination of nitrosoureas. ENU is also readily determined colorimetrically as nitrite after acidic hydrolysis (Preussmann and Schaper-Druckrey, 1972).

Biological Effects (Animal and Human)

1. Absorption: ENU is absorbed and produces toxic effects after ingestion and parenteral administration. It is also likely to be absorbed through the skin in analogy with findings with N-nitroso-N-methylurea.

2. Distribution: Intravenous administration of ^{14}C-ENU to pregnant rats results in distribution of the radiolabel to both maternal and fetal brain and liver in the form of ethylated guanine residues.

3. Metabolism and excretion: The high chemical reactivity of ENU makes it unlikely that an enzymatic metabolism is involved to any significant extent in the activation of ENU. The breakdown of ENU in vivo generates a short-acting carcinogenic intermediate that yields an ethylcarbonium ion that ethylates proteins and nucleic acids. No excretion products have been identified (IARC, 1978).

4. Toxic effects: Acute LD50s for the rat are 240, 240, and 300 mg/kg by the intravenous, subcutaneous, and oral routes, respectively. Target organs in the offspring of pregnant mice are brain (demyelination) and eyes. Bone marrow degeneration occurs in mice after intraperitoneal injection of ENU.

5. Carcinogenic effects: ENU is carcinogenic in all animal species tested. Principal target organs are the central and peripheral nervous system in young rats on oral or subcutaneous administration and the hematopoietic system (resulting in leukemias) on intravenous injection. Older rats also show a high tumor incidence of kidney, uterus, and ovary. In the mouse, the chief target organ is the lung. ENU is especially effective as a transplacental carcinogen.

6. Mutagenic and teratogenic effects: ENU is mutagenic in human lymphocyte and fibroblast cultures and in algae. Teratogenic effects have been noted transplacentally in rats, mice, pigs, and hamsters.

Emergency Treatment

1. Skin and eye exposure: For skin exposure, remove contaminated clothing and wash skin with soap and water. Avoid rubbing of skin or increasing its temperature. For eye exposure, irrigate immediately with copious quantities of running water for at least 15 minutes.

2. Ingestion: Vomiting might reexpose the mouth and esophagus. Drink milk; it may react with nitrosamides. Refer for gastric lavage.

3. Inhalation: Remove victim promptly to clean air. Administer rescue breathing if necessary.

4. Refer to physician.

References

Druckrey, H., R. Preussmann, S. Ivankovic, and D. Schmähl. 1967. Organotropic carcinogenic action of 65 different N-nitroso compounds with BD rats. Z Krebsforschung 69:193-201.

Heyns, K., and H. Roper. 1974. Analysis of N-nitroso compounds. Part 2. Sampling and quantitative determination of homologous N-nitroso-N-alkylureas and N-nitroso-N-alkylurethans by rapid high pressure liquid chromatography. J Chromatogr 93:429-439.

IARC. 1978. IARC Monographs on the Evaluation of Carcinogenic Risk of Chemicals to Humans, Some N-Nitroso Compounds, Vol. 17. World Health Organization, Geneva, Switzerland.

Mirvish, S.S. 1971. Kinetics of nitrosamide formation from alkylureas, N-alkylurethans, and alkylguanidines: Possible implications for the etiology of human gastric cancer. J Natl Cancer Inst 46:1183-1193.

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